

Surgical Approach to Ischemic Mitral Regurgitation Following the First Acute Myocardial Infarction

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Abstract

Background: Ischemic mitral valve regurgitation is a subgroup of secondary mitral valve insufficiency that develops due to ischemic heart disease. The aim of the study is to evaluate the patients who were operated after acute myocardial infarction for the type of interventions to be performed for the mitral valve in terms of mortality and morbidity. **Methods:** It is a single-centered, retrospective study. Patients who were admitted to the hospital with the diagnosis of acute myocardial infarction and operated emergently or urgently between January 2017 and December 2020 were evaluated. Patients who were found to have significant IMR ([?] moderate mitral regurgitation) in the early period and who could achieve complete revascularization were included in the study. Patients were divided into two groups whether the mitral valve was intervened or not. **Results:** The demographical data of the patients that were included in the study is as follows, 73.4% were male and 33% were female. The average age of the patients was 63.2 ± 8.9 . Patients were compared in terms of significant (moderate or higher) postoperative residual mitral regurgitation. 62.2% (n=23) of the patients undergone isolated CABG had mild mitral regurgitation. 5 patients with mitral valve annuloplasty (17.9%) had significant residual regurgitation ($p<0.001$). **Conclusion:** Mitral valve intervention should not be considered in non-severe mitral valve insufficiencies (without papillary rupture or chorda rupture) after acute MI. Preservation of the dynamic structure of the mitral valve annulus in the acute period makes mitral ring annuloplasty not an appropriate treatment.

Introduction:

Ischemic mitral valve regurgitation (IMR) is a subgroup of secondary mitral valve insufficiency that develops due to ischemic heart disease [1]. Although there is no damage to the valvular and subvalvular structures in general, the problem is caused by regurgitation in the valve due to secondary changes in the left ventricular geometry [2,3]. Approximately 12% of patients with coronary artery disease have accompanying moderate or severe mitral valve insufficiency [4]. IMR remains one of the gray zones in cardiac surgery. Current guidelines are still far from clearly formulating a treatment algorithm. The main reason is the complex pathophysiology of IMR with its many treatment options, and the unclear indications for surgical intervention [5]. Recent cardiological studies proved that IMR is not an actual chronic disorder, but it occurs with the first acute myocardial infarction (AMI) [6]. So, it is also not clear whether the current protocols are valid in patients with IMR after AMI because existing pathophysiological findings have been studied only for chronic IMR [6].

The aim of the study is to evaluate the patients who were operated after AMI for the type of interventions to be performed for the mitral valve in terms of mortality and morbidity and to evaluate the residual

regurgitation in the mitral valve.

Material and Methods:

It is a single-centered, retrospective study. In this study, patients who were admitted to the hospital with the diagnosis of AMI and operated after stabilization between January 2017 and December 2020 were evaluated. Among these patients, patients who were found to have significant IMR ([?] moderate mitral regurgitation) in the early period and who could achieve complete revascularization were included in the study. Here, we do not mean the acute complications seen after MI, but patients with echocardiographic IMR findings after AMI. A total of 124 patients meeting the criteria were included in the study.

Patients with primary mitral valve disorders, patients with chordae or papillary muscle rupture, patients with aortic valve intervention, echocardiographic chronic ischemic mitral insufficiency findings, history or previous myocardial infarction and patients who had to undergo incomplete revascularization for any reason were not included in the study.

Patients were divided into two groups as patients who underwent isolated coronary artery bypass grafting (CABG) after acute myocardial infarction (Group 1) and those who underwent mitral valve intervention (mitral valve replacement or mitral ring annuloplasty) in addition to CABG (Group 2).

After comparing the two groups statistically, the patients in Group 2 were divided into two subgroups, those undergoing valve replacement and ring annuloplasty, and subgroup analyzes were performed. The study was approved by the local ethics committee.

Patients were accepted as acute myocardial infarction according to fourth universal definition of myocardial infarction [7]. Patients with fasting blood glucose more than 126 mg / dL (7.0 mmol / L) or HbA1C [?] 6.5% in the preoperative period were considered diabetes mellitus (DM). Patients with systolic blood pressure 140 mmHg and / or diastolic blood pressure [?]90 mmHg in the preoperative period were accepted as hypertension (HT) patients. Patients with Glomerular Filtration Rate (GFR) below 60 ml / min / 1.73 m2 were considered as chronic renal failure. Patients who had routine dialysis with an AV fistula or catheter in the preoperative period were accepted as dialysis patients. Patients with a smoking history of more than 10 pack years were accepted as smokers.

Echocardiographic examinations were used based on the patient files or the preoperative and postoperative echocardiographic examinations in the hospital system. Postoperative echocardiography was performed on the patients in the third postoperative month. Preoperative ejection fractions (EF) of the patients, left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left atrium (LA) diameter, vena contracta (VC), effective regurgitating orifice (ERO), proximal isovelocity surface area (PISA), regurgitating volume (RVol), estimated pulmonary artery pressure (PAP), tenting area, coaptation length, sphericity index, and the amount of insufficiency in the mitral valve were taken. Postoperative EF, LVEDD, LVESD and mitral valve insufficiency were evaluated. Electrocardiograms (ECG) taken preoperatively were evaluated. The postoperative period was evaluated using the daily ECGs taken in the postoperative period and the ECGs when they came to the hospital for postoperative control whether there was any change in rhythm. In the postoperative period, it was evaluated whether there was a newly developed atrial fibrillation (AF) or a permanent pacemaker requirement.

In the perioperative period, cardiopulmonary bypass time and aortic cross clamp times were examined. In the postoperative period, the duration of intensive care hospitalization, the time of leaving the mechanical ventilation, wound infection, and cerebrovascular accidents (CVA) were determined by examining the clinical observation and consultation notes of the patients.

Early mortality was determined as the mortality within the first 30 days after the operation. Ventilation times are calculated in hours. In the postoperative period, if serum creatinine levels increased 1.5 times compared to the basal value or GFR decreased by 25% or more, the patient was accepted as acute kidney injury (AKI). Having received hemodialysis or hemofiltration during the postoperative period, without the need for dialysis before, was accepted as a new-onset dialysis patient.

Statistical Analysis

Statistical results were obtained using IBM Statistical Package for the Social Sciences version 27.0 (SPSS Inc., Chicago, IL, USA) program. Mean, standard deviation, median, lowest, highest, frequency and ratio values were used in the descriptive statistics of the data. The distribution of variables is measured with the Kolmogorov-Smirnov test. Independent sample t-test and Mann-Whitney U test were used in the analysis of quantitative independent data. Chi-square test was used in the analysis of qualitative independent data and Fischer's exact test was used when the necessary conditions for the chi-square test were not met. Univariate analysis was performed to determine statistically significant results related to early mortality risk factors. Binary logistic regression and multivariate analyzes were performed for significant results in univariate analyzes.

Results

The demographical data of the patients that were included in the study is as follows (Table 1), 73.4% (n = 91) were male and 33% were female (n = 33). The average age of the patients was 63.2 ± 8.9 . There is no statistical difference between two groups by the means of demographical data.

The tenting area in Group 2 was significantly higher ($p < 0.05$) than in Group 1. The sphericity index did not differ significantly ($p > 0.05$) between the two groups. Coaptation depth did not differ significantly ($p > 0.05$) between the two groups. Regurgitant fraction in Group 2 was significantly higher than Group 1 ($p < 0.05$). Other echocardiographic data did not differ significantly (Table 2).

The operation time, cardiopulmonary bypass duration and cross clamp time were significantly higher in Group 2 ($p < 0.05$). Also, the length of hospital stay, and ICU stay in Group 2 were significantly higher than Group 1 ($p < 0.05$). No significant difference was found between the two groups for the duration of mechanical ventilation and the use of IABP ($p > 0.05$). In comparison of postoperative complications, no significant difference was found between postoperative CVA development, pneumonia, wound infection, and surgical revision rates ($p > 0.05$). There was no statistically significant difference in mortality between the two groups ($p > 0.05$) (Table 3).

Patients were compared in terms of significant (moderate or higher) postoperative residual mitral regurgitation. 62.2% (n=23) of the patients undergone isolated CABG had mild mitral regurgitation. None of them had any significant residual regurgitation. Patients with CABG+MVR had no residual regurgitation. 5 patients with mitral valve annuloplasty (17.9%) had significant residual regurgitation ($p < 0.001$).

Subgroup Analysis

The group with mitral valve intervention was examined in two subgroups (mitral valve replacement and mitral valve repair). Hypertension rate was significantly higher in MVP group than MVR group ($p < 0.05$). The demographical data between two subgroups didn't differ significantly ($p > 0.05$). Laboratory findings between two subgroups were insignificant. Tenting area was significantly higher in MVR group than MVP group ($p < 0.05$). The VC value in the MVR group was significantly higher ($p < 0.05$) than in the MVP group (Table 4). Perioperative and postoperative data were not significantly different in two subgroups.

Mortality Analysis

Mortality analysis was performed in all patients with mitral regurgitation shortly after acute myocardial infarction. Univariate analyzes were performed to determine early mortality factors. It was found statistically significant that increased age and being a female increased the risk of postoperative early mortality. Cross clamp time was a statistically significant factors affecting mortality. On the other hand, whether the mitral valve was intervened or not was not a significant result.

In the postoperative period, long hospitalization in intensive care unit and long duration of mechanical ventilation are factors that significantly increase mortality. Again, the need for surgical revision, IABP, dialysis and the history of postoperative pneumonia increases the mortality statistically significantly in the

early period. On the other hand, the development of postoperative CVA has not been found to have a significant effect on mortality.

Binary logistic regression analysis was performed for variables that were found to be significant in univariate analyzes. In these analyzes, female gender, duration of mechanical ventilator, need for IABP and need for postoperative dialysis were found to be significant (Table 5).

Discussion

Surgical treatment of heart diseases has been successfully applied worldwide with the developing technology and surgical techniques as of the twentieth century. Mitral valve diseases can also be successfully treated with the pioneering initiatives of the French surgeon Alain Carpentier. Among these, the place of ischemic mitral insufficiency remains a controversial area of cardiac surgery. Even in the light of current guidelines, there is no clear diagnosis and treatment method. The unpredictability of long-term results of the treatments made this subject open to discussion and research.

Although ischemic mitral insufficiency is normally accepted as a part of a chronic ischemic process, recent studies have shown that IMR develops during the first acute MI [6,8,9]. All these studies include primary percutaneous coronary interventions or long-term echocardiographic follow-up. There is no study in the literature about the surgical approach to these patients. On the other hand, the actions to be taken for IMR in the chronic process have not yet been clarified by the guidelines. However, the studies show that these patients should be diagnosed and treated in the acute phase. To the best of our knowledge, our study is the first surgical study on this matter.

Ischemic mitral valve insufficiency is a disease with high mortality rates. Despite effective treatment, long-term mortality rates can vary between 19.8-54% [10,11]. According to some studies, the presence of ischemic mitral insufficiency can increase mortality up to 3 times independent of all factors [12]. The development of moderate and higher ischemic mitral insufficiency causes an increase not only in mortality but also in morbidities [13]. Early surgical mortality rates are also high. In a series, the operative mortality after surgery for patients with moderate ischemic mitral insufficiency was found to be 14% [14], while in another study, the rate was 8% in patients with mitral valve repair and 16% in patients who underwent replacement [15]. Like other studies, our results revealed that early mortality was 16.1% of all patients. In the analysis of the groups, this rate was found to be 17.2% in the group with mitral valve intervention, and 13.5% in patients who underwent isolated CABG. Again, in subgroup analyzes, among patients who had mitral valve intervention, this rate was 20.3% in patients who underwent MVR, while it was 10.7% in patients who underwent MVP. In our study the result was not found to be statistically significant. Increasing the numbers studied will provide significant results.

Acute kidney injury that develops in the postoperative period is a complication that significantly increases both operative mortality and morbidity. In a study conducted by Yamauchi et al, the rate of acute kidney injury after valvular surgery was found to be 6.1%, while Chang et al showed that this rate can increase up to 38.7% after mitral valve surgery [16,17]. Again, in the same studies, it was observed that mortality increased significantly in patients with acute kidney injury. In our study, the postoperative acute kidney injury rate was found to be 25.8%. It was found that 12.19% of all patients needed dialysis in the postoperative period. In our study there was no statistically significant difference in terms of postoperative AKI development or dialysis need, even though it was 3 times more common in patients with mitral valve intervention, mostly the ones with mitral valve replacement. It was determined in our study that the need for dialysis in the postoperative period is an independent risk factor for mortality.

Another important finding in our study is that being a female increases mortality. 26.6% of the patients included in our study consisted of female patients. EuroSCORE II is a scoring system commonly used today to predict mortality. Accordingly, being a female is a situation that increases mortality, and it is seen that female gender increases the risk ratio in scoring [18]. Another study by McNeely et al. showing gender differences in the mitral valve showed that women who needed mitral valve surgery had higher comorbid factors and that woman had a 2.5-fold higher mortality risk in isolated mitral surgery compared to men

[19]. In our study, in univariant analyzes performed to determine early mortality, it was shown that female gender significantly increased the risk more than 2 times ($p = 0.047$). In the multivariant analysis, it was determined in our study that female gender is an independent risk factor for mortality.

Clear mortality factors have not been revealed by the studies conducted. Factors also differ in the long term and early period. For example, early mortality markers according to Dufendach et al. performing mitral valve replacement is DM and preoperative use of IABP. In the long term, different factors such as age, low EF, and COPD have been found [15]. In our study, in univariant analyzes performed to determine the factors determining early mortality, age, female gender, cross-clamp duration, ICU stay time, duration of stay on mechanical ventilator, postoperative dialysis need, IABP and postoperative pneumonia were identified as risk factors. In multivariant analyzes, dialysis need, female gender, IABP and prolonged mechanical ventilator need came to the fore as effective independent factors in determining mortality.

A clear diagnosis of ischemic mitral valve insufficiency is still considered to be challenging today. Keeping the threshold values too low for selecting the type of intervention to be performed will cause unnecessary surgical procedure. On the contrary, keeping the threshold values too high may cause the process to be insufficient. There are even differences in the American Heart Association (AHA) and European Society of Cardiology (ESC) guidelines. While AHA prefers the same echocardiographic measurements as primary mitral insufficiency for advanced secondary mitral insufficiency, ESC increases the limit to 20 for EROA and 30 ml for regurgitant volume [3,20]. Bartko et al. suggested that classical echocardiographic findings would not be sufficient for diagnosis of ischemic MR, and instead a risk-based quantitative measurement are needed. EROA, regurgitating volume and regurgitant fraction should be used collaboratively to diagnose the disease and choose treatment modalities accordingly [21]. In terms of echocardiographic examinations, a study on early stage IMR findings after acute MI was highlighted by Kimura et al. [6]. Accordingly, in the results of our study, when the amount of regurgitation in the mitral valve was examined in the postoperative echocardiography, it was seen that the postoperative regurgitation was the highest in the MVP group. Preservation of mitral annular dynamism in the early period causes the MVP group to have the highest residual regurgitation rate by disrupting the annular morphology starting from the early period. On the other hand, no moderate or higher insufficiency was observed in the postoperative period in any of the patients who underwent isolated CABG. While there was no residual regurgitation in 37.8% of the patients, 62.2% had trace or mild regurgitation. On the other hand, when MVR and MVP were compared, it was found that residual leakage was significantly higher in those who had MVP. While 14.3% of the patients who underwent MVP had moderate insufficiency, 3.6% of them had severe insufficiency. Therefore, MVP for mitral insufficiency in patients operated in the early period after acute MI is not considered an appropriate treatment method.

The study of Sandoval et al. showed us that there is no difference in long-term mortality in patients with moderate IMR compared to patients who underwent isolated CABG with CABG and ring annuloplasty. Isolated CABG has lower operative mortality risks. Cardiopulmonary bypass and cross clamp times are shorter. There are fewer rhythm problems and complications. Hospital and intensive care stay periods have also been found to be shorter [22]. In parallel with these studies, the operation time, cardiopulmonary bypass times and cross clamping times were significantly shorter in patients who underwent isolated CABG compared to patients who underwent mitral valve intervention ($p < 0.005$). Hospital stay and ICU stay are also significantly shorter in CABG patients ($p < 0.005$). On the other hand, in the comparison of the patients who underwent MVR and MVP, no significant difference was found between the operation time, cardiopulmonary bypass time and cross clamp times. Again, there was no difference between hospitalizations and ICU admissions. These results led us to the conclusion that MVP is not a good alternative for patients to be operated after acute MI. There are also studies showing that it can be used safely used in patients with chronic moderate IMR and the left ventricular remodeling is better in the postoperative period [23]. However, the lack of studies on IMR after acute MI and the study showing that the preserved dynamism of the mitral annulus structure [6], the use of ring annuloplasty in patients with IMR after acute MI does not seem appropriate. Recent study of Haberman et al [24] showed that mitral regurgitation following acute myocardial infarction has high mortality rates and early intervention to this patient group has promising

results. They claimed that mitral intervention had better results compared to conservative treatment options.

There are many limitations to this study. The main limitation is the retrospective nature of our study. All data related to patients were scanned retrospectively from hospital information systems. However, the guidelines lack evidence in acute situations, so it is hard to conduct a prospective study on the matter. The fact that there are more than one surgical team in our hospital and that there is no clear preference regarding the types of operation in the guidelines does not allow an operation in accordance with a fixed protocol. We tried to recruit patients who had a myocardial infarction for the first time in this study. We made the patient selection based on the history and applications of the patients, so this is an important limitation of the study. It is a single center study. In addition to the current study, conducting multi-center prospective studies in which the number of patients is increased will provide more significant and guiding results.

Conclusion

Our study is one of the few studies conducted on interventions for ischemic mitral valve insufficiency after AMI and their results. Although the mechanisms and details of chronic IMR are known, the uncertainty of treatment methods keeps this subject open as a research area. Recent studies reveal that the pathophysiology of IMR begins to develop in the first hours after acute MI and early intervention may be beneficial in terms of reversibility. Mitral valve intervention should not be considered in non-severe mitral valve insufficiencies (without papillary rupture or chorda rupture) after acute MI. In conclusion, we believe that isolated coronary artery bypass grafting surgery is a more appropriate option for patients with moderate insufficiencies. Valve replacement should be considered as the first choice in the early period if it is considered to intervene with the mitral valve.

Author Contributions:

Barış Timur: concept/design, drafting article

Gamze Babur Güler: concept/design, critical revision of article, approval of article

Tugba Aktemur: data analysis

Zihni Mert Duman: data analysis, statistics

Timuçin Aksu: critical revision of article

Zinar Apaydın: data collection

Emine Aleyna Eroğlu: data collection

Taner İyigün: critical revision of article, approval of article

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